IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re: Reiner Rygiel Confirmation No: 2780

Serial No: 10/694,287 Group: 2872

Filed: October 27, 2003 Examiner: Pritchett,

Joshua L.

For: Sample Carrier for a Confocal

Microscope and Method for Fabricating a Sample Carrier

Customer No.: 29127

Attorney 21295.65 (H5680US)
Docket No.

AFTER FINAL AMENDMENT UNDER RULE 116

VIA FACSIMILE: 571-273-8300

Mail Stop AF

Commissioner for Patents

P.O. Box 1450

Alexandria, Virginia 22313-1450

Sir:

In response to the pending final Office Action, mailed March 21, 2006 (Paper No. 920060316), please amend the above-captioned patent application as follows:

-amendments to the claims are reflected in the listing of claims in section a;

Finally, reconsideration is requested in view of the remarks set forth in section b.

Application No.: 10/694,287 Amendment dated: June 21, 2006 Reply to Office Action of March 21, 2006 Attorney Docket No.: 21295.65 (H5680US)

This listing of claims will replace all prior versions and listings of claims in this application:

a) Listing of Claims

What is claimed is:

- 1. (Previously presented) A sample carrier for a confocal microscope, comprising: a first coverslip and a second coverslip, wherein the second coverslip carries a mirror; wherein the mirror surrounds a sample region which is defined on the second coverslip; a frame which holds the first and the second coverslip and thereby provides a cavity between the first and the second coverslip; a medium filled in the cavity, which has approximately the same refractive index as the first and the second coverslip.
- 2. (Original) The sample carrier as defined in Claim 1, wherein the substrate of the first and the second coverslip is made of anisotropic or isotropic materials that are transparent to the wavelengths used.
- 3. (Original) The sample carrier as defined in Claims 1, wherein the first and the second coverslip are made of quartz glass; and the medium in the cavity is glycerol.
- (Original) The sample carrier as defined in Claim 3, wherein the distance between the first and the second coverslip is no greater than 50 μm.
- 5. (Original) The sample carrier as defined in Claim 1, wherein the mirror on the second coverslip is made from a material that acts reflectively for light in a wavelength region between $\lambda = 300$ nm 1300 nm.
- 6. (Original) The sample carrier as defined in Claim 5, wherein the material of the mirror is aluminum or silver with a protective layer, or gold.

Application No.: 10/694,287

Amendment dated: June 21, 2006

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Attorney Docket No.: 21295.65 (H5680US)

7. (Original) The sample carrier as defined in Claim 5, wherein the mirror is made of a

dielectric mirror coating.

8. (Original) The sample carrier as defined in Claim 1, wherein the mirror is embodied

as a circular ring around the sample region.

9. (Original) The sample carrier as defined in Claim 1, wherein at least the first or the

second coverslip is secured to the frame using a special adhesive.

(Original) The sample carrier as defined in Claim 1, wherein the first and the

second coverslip are in the shape of a circle.

11. (Original) The sample carrier as defined in Claim 1, wherein the first and the

second coverslip possess the shape of a polygon with sides of identical length.

(Original) The sample carrier as defined in Claim 1, wherein the first and the 12.

second coverslip are in the shape of a rectangle.

(Original) The sample carrier as defined in Claim 1, wherein the microscope is a

interferometric fluorescence microscope, such as 4-pi microscope, standing wave

field microscope, I²M, I³M, and I⁵M microscope, and theta microscope.

Claims 14-19 - Cancelled

3 of 5

Application No.: 10/694,287 Amendment dated: June 21, 2006 Reply to Office Action of March 21, 2006 Attorney Docket No.: 21295.65 (H5680US)

b.) Remarks

Claim 1-13 have been rejected. Claims 14-19, previously withdrawn from consideration, have been cancelled.

Claims 1, 2, 4, 5 and 7-13 were rejected under 35 U.S.C. §103(a) over Bewersdorf (U.S. Patent Application Publication No. 2002/0105722) in view of Eastman (U.S. Patent No. 6,411,434). Claim 3 was rejected under 35 U.S.C. §103(a) Bewersdorf (U.S. Patent Application Publication No. 2002/0105722A1) in view of Eastmann (U.S. Patent No. 6,411,434) as applied to Claim 1 above, and further in view of Lakowicz (U.S. Patent Application Publication No. 2002/0160400A1). Claim 6 was rejected under 35 U.S.C. §103(a) over Bewersdorf (U.S. Patent Application Publication No. 2002/0105722A1) in view of Eastman (U.S. Patent No. 6,411,434) as applied to Claim 1 above, and further in view of Aagard (U.S. Patent No. 3,720,924).

Although the Patent Office did not state under which section 102/103(a) the obviousness rejections were made, Applicant asserts that Bewersdorf cannot be cited against the referenced claims.

In particular, if the 103(a) rejection asserted Bewersdorf as a section 35 U.S.C. 102(e)/103(a) citation, Applicant points out that Bewersdorf and the present application are commonly assigned to Leica Microsystems Heidelberg. A copy of the assignment record of the present application to the common assignee in the US PTO is enclosed with this response. A copy of the assignment of the Bewersdorf application to the same common assignee is enclosed with this response. Under 35 U.S.C. 103(c)(1) commonly assigned subject matter in Bewersdorf cannot be cited against the claimed invention in the present application assigned to the same assignee under section 102(e)/103(a).

Alternatively, if the Patent Office has asserted Bewersdorf as a 35 U.S.C. 102(a)/103(a) citation, Applicant respectfully submits a Declaration under 37 C.F.R. 1.131 (enclosed with this response), establishing the date of conception and reduction to

Application No.: 10/694,287

Amendment dated: June 21, 2006

Reply to Office Action of March 21, 2006

Attorney Docket No.: 21295.65 (H5680US)

practice of the claimed invention no later than July 23, 2002, which is earlier than the

August 8, 2002 publication date of Bewersdorf. Therefore, the published Bewersdorf

application cannot be cited against Applicant's claims even under 35 U.S.C.

102(a)/103(a).

Thus, the 103(a) rejections in the present application should be withdrawn and

Claims 1-13 should be allowed.

Applicant believes that the present application is in condition for allowance. A

Notice of Allowance is respectfully solicited. Should any questions arise, the Examiner

is encouraged to contact the undersigned.

Respectfully submitted,

HOUSTON ELISEEVA LLP

/Maria Eliseeva/

By:

Maria Eliseeva

Reg. No. 43,328

4 Militia Drive, Suite 4

Lexington, MA 02421 Phone: 781-863-9991

Fax: 781-863-9931

Date: June 21, 2006

Unser Zeichen

P2376



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	Verfahren zur Unte	rsuchung ei	ner Probe								
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4) Welche technische Aufgabe liegt der Erfindung zugrunde (Zielsetzung, Vorteile, Verbesserung)?

Durch den erfindungsgemäßen Randspiegel in der Probenebene sind Justagen und nachfolgende Probenbetrachtungen in Einem möglich, ohne dass die Probe ausgebaut werden muss. Der Randspiegel hillt im Besonderen bei Interferometrischen Verfahren in der Fokalebene im konfokalen Mikroskopaufbau. Des Weileren lässt sich eine Probe zielgerichteter aufbringen ohne große Spiegelflächen durch die Probe zu verunreinigen. Durch die verschiedenen Oberflächen Spiegel- Glas kommt es zu einer Veränderung der Oberflächenspannung, bei flüssig aufgebrachten Proben, so dass dadurch die Probe in der Mitte des Probenraum gehalten werden kann. Auf zusätzliche Maßnahmen wie Spacer kann also verzichtet werden.

5a) Welcher Stand der Technik ist Ihnen bekannt?

Leica-Anmeldung DE 101 00 247, unser Aktenzeichen: A 2876 DE

Bisher werden Objektdeckgläser benutzt, bei denen eine Hälfte des Probenraums ist halbmondartig verspiegelt. Eine andere Methode besteht darin, kleine Spiegelplättchen verteilt in die Probe einzubringen.

5b) Welche Nachteile oder Mängel gegenüber der Erfindung welst der Stand der Technik auf?

Nachteilig in der bisherigen konfokalen Mikroskopie ist die Entnahme von Justagemitteln, aus der Fokalebene, die eine nachfolgende Betrachtung von Proben mit den eben vorjustiertem Mikroskop erschwert, bzw. unsicher macht, weil melst der Aufbau dadurch verändert worden ist.

Die halbseitig verspiegelten Deckgläser haben den Nachteil, dass der Anwender häufig Schwierigkeiten hat, die verspiegelte Fläche zu finden. Außerdem ist der Probenbereich so groß, dass die Probe häufig nicht gut lokalisiert werden kann.

Die Methode mit den Spiegelplättchen ist nicht geeignet, da die Plättchen schwer zu finden sind und auch zerstöranfällig sind.

6) Ausführliche Beschreibung der Erfindung einschl. Zeichnung und/oder Handskizze; evtl. auch andere Lösungsmöglichkeiten skizzieren. Welche Merkmale sollen unter Schutz gestellt werden?

Auf einem Probenträgersubstrat ist ein Randspiegel so aufgebracht, das, dieser einen Freiraum in der Mitte des Probenträgers lässt. In diesem freibleibenden Bereich können aufgebrachte Proben, orthogonal zur Probenebene, von beiden Seiten in einer Fokalebene eines konfokalen Mikroskops betrachtet werden. An dem Randspiegel könnten zur gleichen Zeit Interferenzversuche zur Justage eines Interferometrischen Aufbaus durchgeführt werden, wie zum Beispiel ein Wellenfrontenvergleich zweier Wellenfronten, die jeweils von einer der Spiegelselten reflektiert werden und deren Phasenbeziehungen zueinander verglichen werden können.

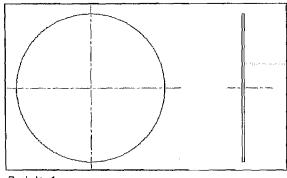
Insbesondere soll dieser Aufbau für Systeme geschützt werden, in denen interferometrische Verfahren in der konfokalen Fluoreszenz-Mikroskople eingesetzt werden, wie 4Pi und ¹⁹M- sowie Theta-Mikroskople, usw.

Der Aufbau des Probenträgers mit Randspiegel besteht aus

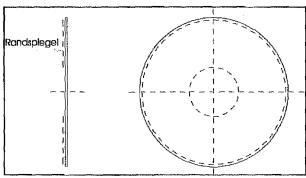
- 1. Deckglas 1, wobei das Substrat aus allen anisotropen oder isotropen klaren Materiallen bestehen kann
- 2. Deckgtas 2, wobe) das Substrat aus allen anisotropen oder isotropen klaren Materiallen bestehen kann, auf diesem ist zusätzlich ein Randspiegel aufgebracht. Das Randspiegelmaterial kann aus allen Materialen bestehen, für die Reflektion vorhanden ist, in einen Wellenlängenbereich von $\lambda = 300$ nm 1300nm.

Beispielswelse kann der Spiegel aus einer Silberschicht mit Schutzschicht oder aus einer einfachen Goldschicht bestehen.

Die verspiegelte Schicht befindet sich kreisförmig um den elgentlichen Probenraum herum. Das hat den Vortell, dass beim Verfahren des Probenträgers senkrecht zur optischen Achse zu irgendeinem Randbereich hin, die optische Achse immer eine verspiegelte Zone treffen wird. Das ist zum Abgleich der Justage sehr wichtig und nützlich.



Deckglas 1
Funktionsansicht



Deckglas 2 mit Randspiegel

Weiterhin sollte ein Verfahren zur Probenpräparation geschützt werden.

Zunächst wird eine wässrige Probe (ca. 1 µl) auf den Freiraum in der Probenträgermilte aufgebracht. Da es sich um eine wässrige Probe handelt, blidet diese einen Tropfen und benetzt nicht die Verspiegelung. Die Probe wird anschließend mittels eines Trocknungsverfahrens behandelt. Das Wasser verdunstet und die eigentliche Probe bleibt am Probenträger kleben. Danach wird eine definierte Menge von z.B. Glyzerin (z.B. 1 µl) auf die Probe aufgebracht und die beiden Deckgläser werden anschließend übereinander gebracht und fest mitleinander verbunden. Dazu werden die übereinanderliegenden Deckgläser in einen Rahmen gelegt und mit einem Spezialkleber fixiert. Das Glyzerin verteilt sich dann ganz gleichmäßig in dem Zwischenraum, so dass überall nahezu der gleiche Brechungsindex vorhanden ist. Es hat sich herausgestellt, dass für eine 4-Pi-Anwendung der Probenraum nicht dicker als 50 µm sein solite.

Es kann auch ein anderes Medium als Glyzerin verwendet werden. Wichtig ist nur, dass im gesamten Raum zwischen den Objektiven nur wenig Brechungsindexschwankungen vorhanden sind.

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+49 ((0)6441-29-2223 Dr.	W. F. Reichert	1		25/07/02			

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CONFIDENTIAL - INVENTION DISCLOSURE

Our ref.:

P2376 (please indicate on any correspondence)

5 To Patent Coordinator

BU: LLT

Dr. Kyra Möllmann

Date received/Signature

July 23, 2002

//signature//

10

Forward to:

Leica Microsystems AG

Corporate Patents + Trademarks Department (CPTD)

Date received/Initials

July 25, 2002 //initials//

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1) Subject matter of the Invention Disclosure (e.g. Device for, Equipment for, Apparatus for, Device for, Component for, Method for, or the like):

Specimen coverslips for microscopy, in particular 4-pi microscopy, and method for investigating a sample

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2) The following is/are involved in the creation of the invention as inventors (if additional space is needed, fill out a further Invention Disclosure):

Last name, first name

Rygiel, Reiner

Professional qualification

Dipl.-Ing.

25 Business Unit

LLT

Corporate function and position

Project manager

Telephone

0621 7028 2023

Nationality

D

Percentage

100

30 Home address

Ziegeleistr. 123

D-67122 Altrip

3) The invention was created (indicate separately for each inventor):

H 5680 US

By observations of the inventor himself (e.g. recognition of shortcomings).

I affirm that to my knowledge the information is accurate and complete and that additional persons are not involved in the invention, and that that no previous uses or publications of the disclosed invention are known to me.

Inventor A

Place/Date Mannheim, July 23, 2002

Inventor's signature //signature//

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4) What is the technical object on which the invention is based (objective, advantages, improvement)?

The edge mirrors according to the present invention in the sample plane make possible alignments and subsequent sample observations together, with no need to remove the sample. The edge mirror helps in particular with interferometric methods in the focal plane in a confocal microscope configuration. It is also possible to mount a sample in more targeted fashion without contaminating large mirror surfaces with the sample. The different surfaces (mirror, glass) result in a change in surface tension in the context of samples applied in liquid form, so that the sample can thereby be kept in the center of the sample space. It is thus possible to dispense with additional features such as spacers.

5a) What prior art are you aware of?Leica Application DE 101 00 247, our file no.: A 2876 DE.

Specimen coverslips in which one half of the sample space is mirror-coated in half-moon fashion have hitherto been used.

Another method consists in introducing small mirror-coated flakes into the sample in distributed fashion.

30 5b) What disadvantages or shortcomings does the prior art exhibit as compared with the invention?

A disadvantage in previous confocal microscopy is the removal of alignment means from the focal plane; this complicates, or makes unreliable, subsequent 5

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observation of samples using the microscope that has just been prealigned, since the assemblage has usually been modified thereby.

The coverslips that are mirror-coated on one half have the disadvantage that the user often has difficulty finding the mirror-coated surface. The sample region is moreover so large that the sample often cannot be readily located.

The method using the mirror-coated flakes is not suitable because the flakes are difficult to find and also susceptible to damage.

6) Detailed description of the invention, including drawings and/or sketches; also sketch other possible solutions if applicable. Which features should be protected?

An edge mirror is mounted onto a sample carrier substrate in such a way that the mirror leaves an open space at the center of the sample carrier. In this region that is left open, applied samples can be viewed, orthogonally to the sample plane, from both sides in a focal plane of a confocal microscope. Interference experiments for alignment of an interferometric assemblage could be performed at the same time on the edge mirror, for example a wave-front comparison of two wave fronts which are each reflected from one of the mirror sides and whose phase relationships can be compared with one another.

This assemblage is to be protected, in particular, for systems in which interferometric methods are used in confocal fluorescence microscopy, such as 4-pi and I⁵M microscopy, theta microscopy, etc.

The assemblage of the sample carrier with edge mirror comprises:

- 1. Coverslip 1, in which context the substrate can consist of any anisotropic orisotropic clear material;
 - 2. Coverslip 2, in which context the substrate can consist of any anisotropic or isotropic clear material; an edge mirror is additionally applied on the coverslip. The edge mirror material can consist of any material for which reflection exists in a wavelength range from λ = 300 nm to 1300 nm.

The mirror can consist of, for example, a silver layer having a protective layer, or a single gold layer.

The mirror-coated layer is located in a circle around the actual sample space. This has the advantage that upon displacement of the sample carrier perpendicular

to the optical axis toward any edge region, the optical axis always encounters a mirror-coated zone. This is very important and useful for adjusting the alignment.

Coverslip 1

5 Functional view

Coverslip 2 with edge mirror

Edge mirror

10 A method for sample preparation should also be protected.

Firstly an aqueous sample (approx. 1 µl) is applied onto the open space at the center of the sample carrier. Because the specimen is aqueous, it forms a droplet and does not wet the mirror coating. The sample is then treated by means of a drying method. The water evaporates and the actual sample remains adhered to the sample carrier. A defined quantity of, for example, glycerol (e.g. 1 µl) is then applied to the sample, and the two coverslips are then placed against one another and fixedly joined to one another. For that purpose, the coverslips laid on top of one another are placed into a frame and immobilized with a special adhesive. The glycerol is then very uniformly distributed in the interstice, so that almost the same refractive index is present everywhere. It has been found that for 4-pi use, the sample space should be no thicker than 50 µm.

A medium other than glycerol can also be used. All that is important is that very few refractive index fluctuations exist in the entire space between the objectives.

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Immersion medium

Coverslip 1

Sample space

Mirror

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Coverslip 2

This view is a Z-vector depiction

- 7) The following documents are constituents of this Invention Disclosure:
 Drawings 2 sheets
- 8) General information about the invention submitted
- 5 a) Do applications of the invention exist or are they envisioned?

 Yes (Which? Project?)
 - b) Have publications, papers, communications to third parties, exhibits, presentations, or deliveries related to it already occurred?

No

10 c) Is the invention part of a publicly funded project?

No

CPTD receipt confirmation

Date

July 25, 2002

15 Signature

//signature//

Dr. Werner F. Reichert

Assigned patent specialist

Telephone

+49 (0)6441-20-2223

Name

Dr. W.F. Reichert

20

We expressly remind you of your obligation to keep the disclosed invention confidential until official application for a protective right, or until express authorization for disclosure by the Corporate Patents + Trademarks Department (CPTD)!

25

Date/Signature

//signature// July 25, 2002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re:

Reiner Rygiel

Confirmation No:

2780

Serial No:

10/694,287

Group:

2872

Filed:

October 10, 2003

Examiner:

Pritchett, Joshua L.

For:

Sample Carrier for a Confocal Microscope, and Method for

Fabricating a Sample Carrier

Attorney Docket No. 21295.65 (H5680US)

DECLARATION OF PRIOR INVENTION UNDER RULE 37 CFR 1.131

I, being warned of the penalties for perjury, hereby declare and make the following statements:

- The Patent Office cited U.S. 2002/0105722 to Bewersdorf (published on August 8, 2002) in rejecting Claims 1-13 in the above-referenced application under 35 U.S.C. 103(a).
- 2. The invention claimed in the above-referenced U.S. patent application Serial Number 10/694,287 was conceived and reduced to practice by inventor Reiner Rygiel in Germany, a WTO country, as evident from the copy of the invention disclosure form enclosed with this Declaration.
- I am fluent in German and English and I attest that it is evident from the copy of the invention disclosure that it was signed and submitted by Reiner Rygiel to the Corporate Patent and Trademark Department (CPTD) of Leica Microsystems AG, now Leica Microsystems GmbH, the holding of Leica Microsystems Heidelberg GmbH, now Leica Microsystems CMS GmbH, his employer and the assignee of the present invention, on July 23, 2002. The

receipt of the invention disclosure was acknowledged on July 25, 2002 by Dr. Werner F. Reichert, then the Director of the CPTD of Leica Microsystems AG. Therefore, the invention was conceived and reduced to practice no later than July 23, 2002.

Leica Microsystems GmbH

Corporate Patent and Trademark Department

Michael Stahl

Patent Specialist



United States Patent and Trademark Office

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Assignments on the Web > Patent Query

Patent Assignment Abstract of Title

NOTE: Results display only for issued patents and published applications. For pending or abandoned applications please consult USPTO staff.

Total Assignments: 1

Publication #: US20040087006 Pub Dt: 05/06/2004

Inventor: Reiner Rygiel

Title: Sample carrier for a confocal microscope and method for fabricating a sample carrier

Assignment: 1

Conveyance: ASSIGNMENT OF ASSIGNORS INTEREST (SEE DOCUMENT FOR DETAILS).

Assignor: RYGIEL, REINER Exec Dt: 10/10/2003

Assignee: LEICA MICROSYSTEMS HEIDELBERG GMBH

AM FRIEDENSPLATZ 3

MANNHEIM, GERMANY D-68165

Correspondent: HOUSTON ELISEEVA

4 MILITIA DRIVE, SUITE 4 LEXINGTON, MA 02421

Search Results as of: 06/21/2006 10:48 AM

If you have any comments or questions concerning the data displayed, contact OPR / Assignments at 571-272-3350

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